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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/285,531	04/02/1999	YUTI CHERNAJOVSKY	KIR95-01A	3818

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EXAMINER	
O HARA, EILEEN B	
ART UNIT	PAPER NUMBER
1646	23

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/285,531	CHERNAJOVSKY ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 August 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *26 August 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-3, 6, 8, 14-17 and 19-37*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because: Applicants argue that the claimed receptor shows surprising advantages over other multi-TNF receptor-based molecules, that the instant molecule, as exemplified by Hu TNF-R75 ECD, shows the same anti-TNF-specific activity as an Ig-based TNF receptor molecule and at only a third of the concentration required for the Ig-based molecule, and that the molecule is characterized by a low molecular weight, an optimal linker length, and the absence of an Ig Fc domain which has the potential to cause side effects. Applicants argue that these features combined make this molecule unexpectedly superior to known TNF receptor-based molecules. Applicants assert that the Examiner has failed to make a prima facie case of obviousness, that the cited references when combined must teach or suggest every element of the claims, one of ordinary skill must have been motivated to combine the teachings of the references at the time of the invention, and there must be a reasonable expectation of success, and reiterate their remarks made in the October 15, 2001 Amendment. Applicants' arguments have been fully considered but are not deemed persuasive, for reasons cited in the previous office actions, Paper No. 18 at pages 5-7 Paper No. 8, at pages 2-4, and Paper No. 20 at pages 2-6. Wallach et al. teach that a multimer may be produced by recombinant technologies, and provides ample guidance in Example 4 that such methods were known and practiced by one of ordinary skill in the art, and at column 4, lines 19-21, Wallach et al also stated "Those of ordinary skill in the art will be able to determine the optimum length of any such linker molecules to produce multimers which best bind to the TNF trimer." At lines 31-33, Wallach et al state that "the optimum length of such linkers in such recombinantly produced proteins can also be determined by routine experimentation." From these statements, it can be reasonably interpreted by the skilled artisan that Wallach et al. teaches that the particular amino acids in the linker are not critical, but that the length for optimum activity is important and can be determined experimentally by one of ordinary skill in the art. Though the specific linker length of 10-30 amino acids is not specifically taught, one of ordinary skill in the art would expect to have to experimentally test different linker lengths in order to find an optimal linker length. Even if the molecule of the instant invention has greater activity compared to a comparable receptor multimer comprising an Fc domain, is smaller than a receptor multimer comprising an Fc domain, and is less immunogenic than a receptor multimer comprising an Fc domain, these features of the claimed receptor are not surprising or unexpected. Given the state of the art at the time of the invention, these are characteristics that the skilled artisan would have attempted to produce in such a molecule. The skilled artisan would have been motivated to construct such receptor multimers, because proteins having greater activity and fewer side effects are desirable. The Wallach and Smith references provided ample guidance to construct such improved compounds, and experimentation to improve therapeutic compounds was routine in the art at the time of the invention. Such experimentation was routine in the art at the time of the invention, and the skilled artisan would have had a reasonable expectation of success of developing therapeutic compounds with improved characteristics. Therefore, the rejection under 35 USC § 103 is maintained.